

# NEUROPEPTIDI

# NEURONI PEPTIDERGICI

- I neuroni produttori di peptidi non si trovano solamente nell'ipotalamo, ma in tutto il SNC
- I neuropeptidi hanno il ruolo di neuromodulatori nella trasmissione sinaptica
- I recettori per i peptidi si trovano in diverse regioni dell'encefalo, anche distanti dai terminali peptidergici, in questo caso si pensa che agiscano attraverso meccanismi paracrini (volume transmission)
- I neuropeptidi inoltre influenzano molti comportamenti, per cui la loro azione parormonale si rivolge essenzialmente ai circuiti cerebrali

# FAMIGLIE DI NEUROPEPTIDI

TABLE 1

Families of Structurally and Functionally Related Peptides

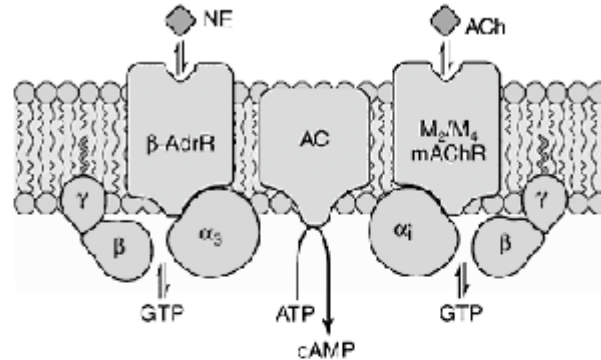
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- (1) VIP, secretin, glucagon, GIP, PHI, GRF
  - (2) Neurotensin, pancreatic polypeptide
  - (3) Cholecystokinin, gastrin, cerulein, phyllocerulein
  - (4) Vasopressin, oxytocin, vasotocin, etc.
  - (5) a. Bombesin, alytesin  
b. Ranatensin, litorin
  - (6) Tachykinins: eledoisin, physalaemin, uperolein, phyllomedusin, kassinin, chylambatin, substance P
  - (7) a. ACTH, MSH, LPH, endorphins, Met-enkephalin  
b. Leu-enkephalin, dynorphin, alpha- and beta-neo-endorphins, etc.
  - (8) Kinins
  - (9) Angiotensins
  - (10) Sauvagine, CRF
  - (11) Somatostatin, urotensin II
  - (13) Kyotorphin, neo-kyotorphin
  - (14) Atrial and brain natriuretic peptides
  - (15) Growth hormone, prolactin
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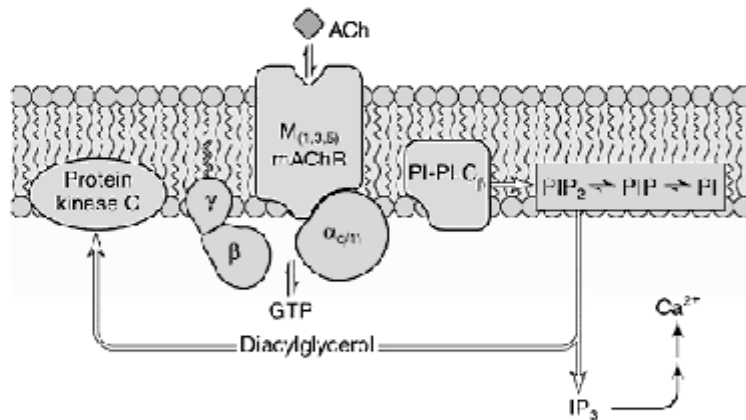
# RECETTORI PER I PEPTIDI

Primary biochemical responses  
mediated by muscarinic acetylcholine receptors

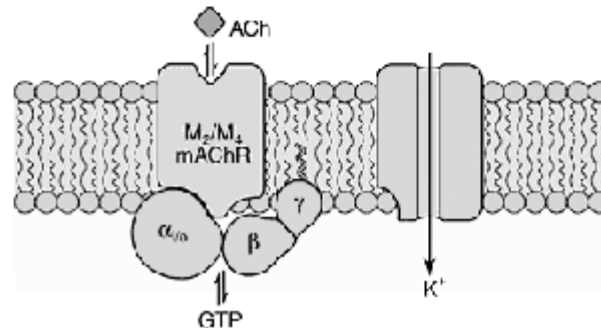
Inhibition of  
adenylyl cyclase



Stimulation of  
phospholipase C



Regulation of  
K<sup>+</sup> channels



I recettori per i neuropeptidi sono del tipo *transmembrana*. Attivano quindi una cascata di eventi metabolici intracellulari che possono influenzare non solo il potenziale di membrana, ma anche il metabolismo cellulare.

# STUDI ATTUALI SUI NEUROPEPTIDI

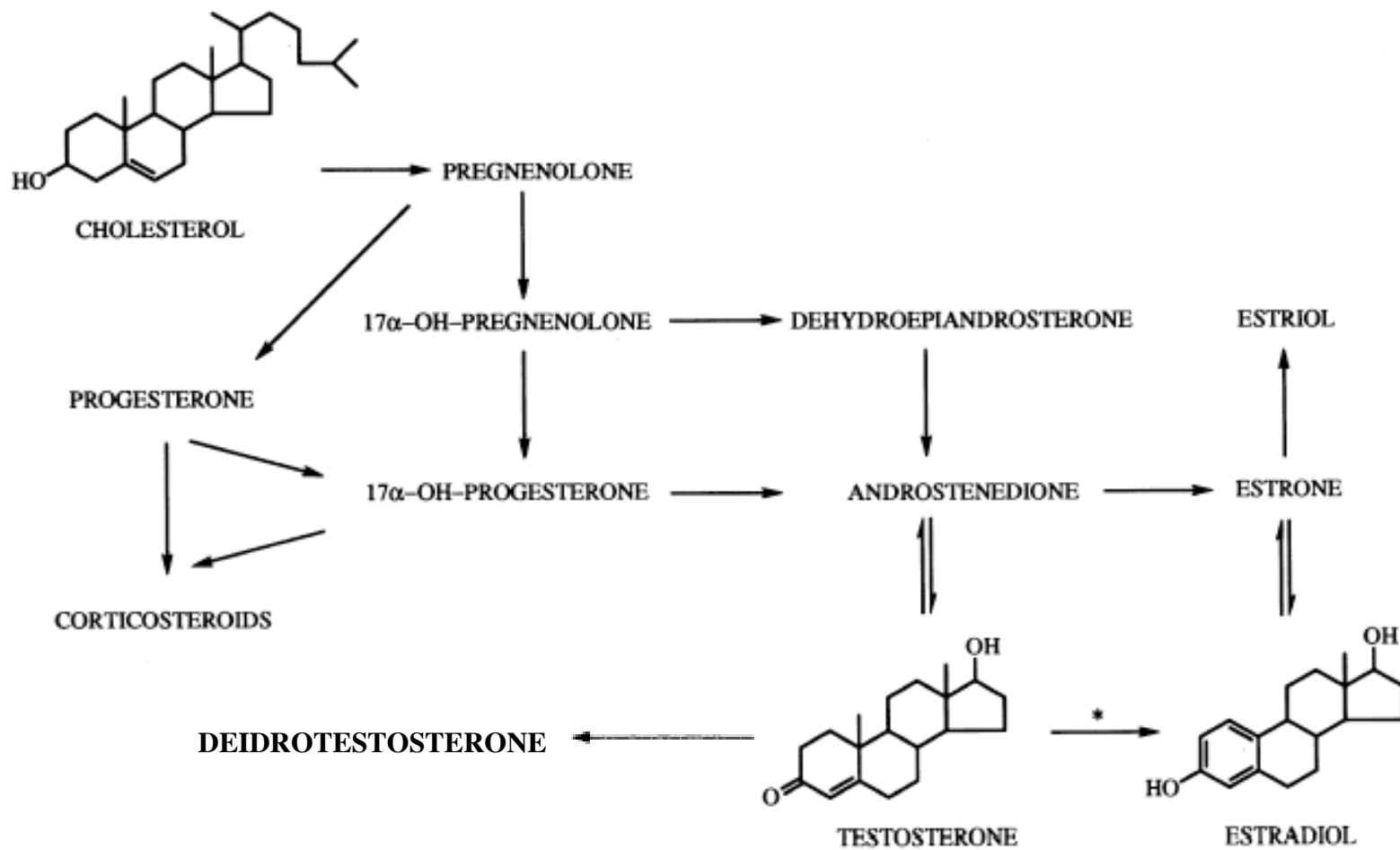
- (1) studies on neurotropic and behavioral actions of neuropeptides;
- (2) studies on physiological and pharmacological actions of neuropeptides;
- (3) studies on the mechanisms of action (including studies on receptors; receptor solubilization; the most promising technique is cloning of receptor cDNAs);
- (4) structure–activity studies, construction of synthetic analogs with predicted properties;
- (5) studies on neuropeptide localization and colocalization;
- (6) studies on neuroendocrine tumors;
- (7) molecular biology of neuropeptides and their life cycles, including processing by specific peptidases;
- (8) studies on neuropeptide-specific peptidases, including search for their specific activators and inhibitors as possible tools of regulation of the level of neuropeptides in the organism;
- (9) studies on neuropeptides in lower animals and in evolution;
- (10) neuroimmunoendocrinology.

# **NEUROSTEROIDI**

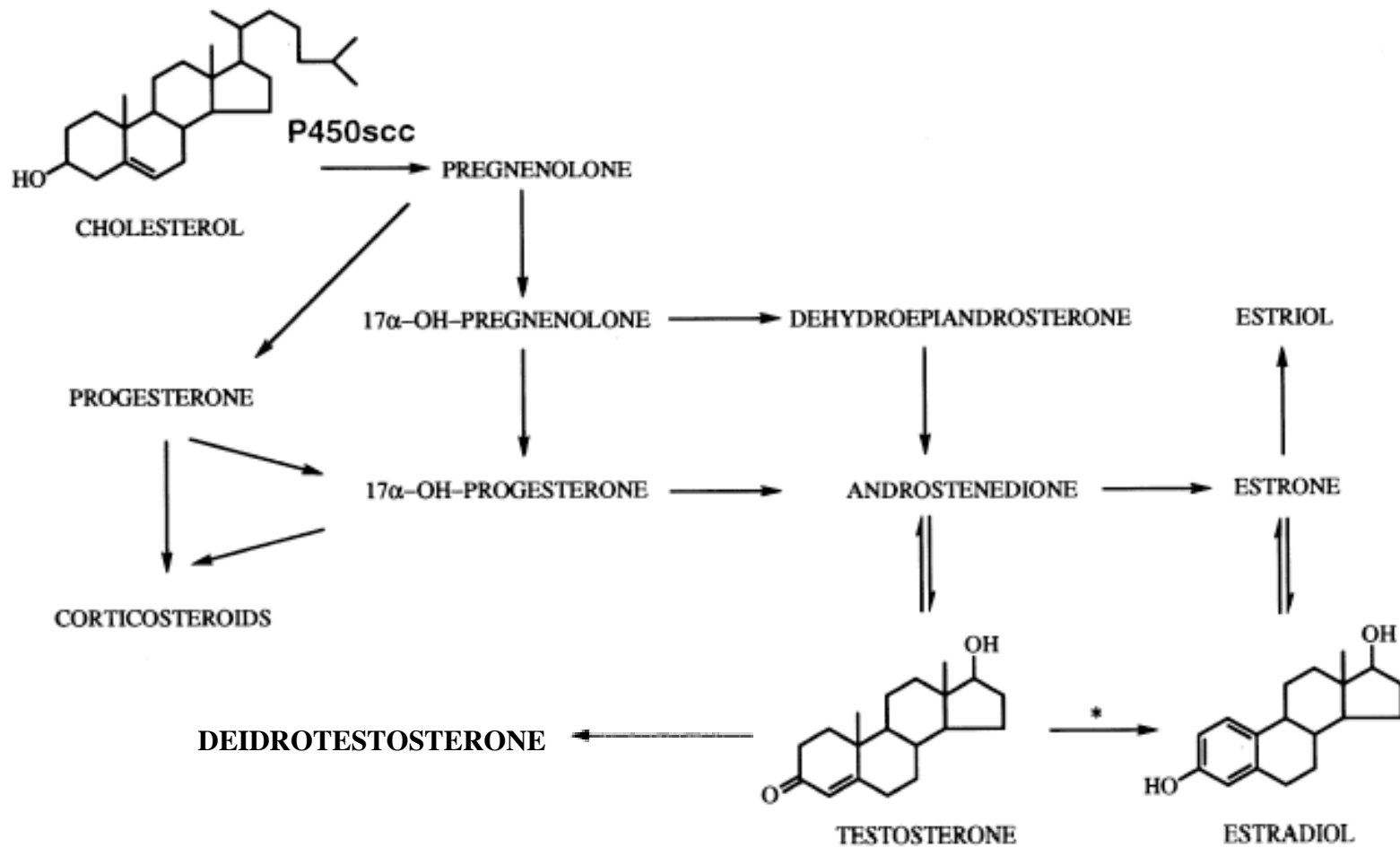
# SIGNIFICATO DEL TERMINE

- Steroidi sintetizzati all'interno del sistema nervoso centrale (neuroni o glia)
  - Distinzione tra neosintesi e metabolismo
  - Azione "solo" sul SNC?
- Steroidi neuroattivi

# SINTESI

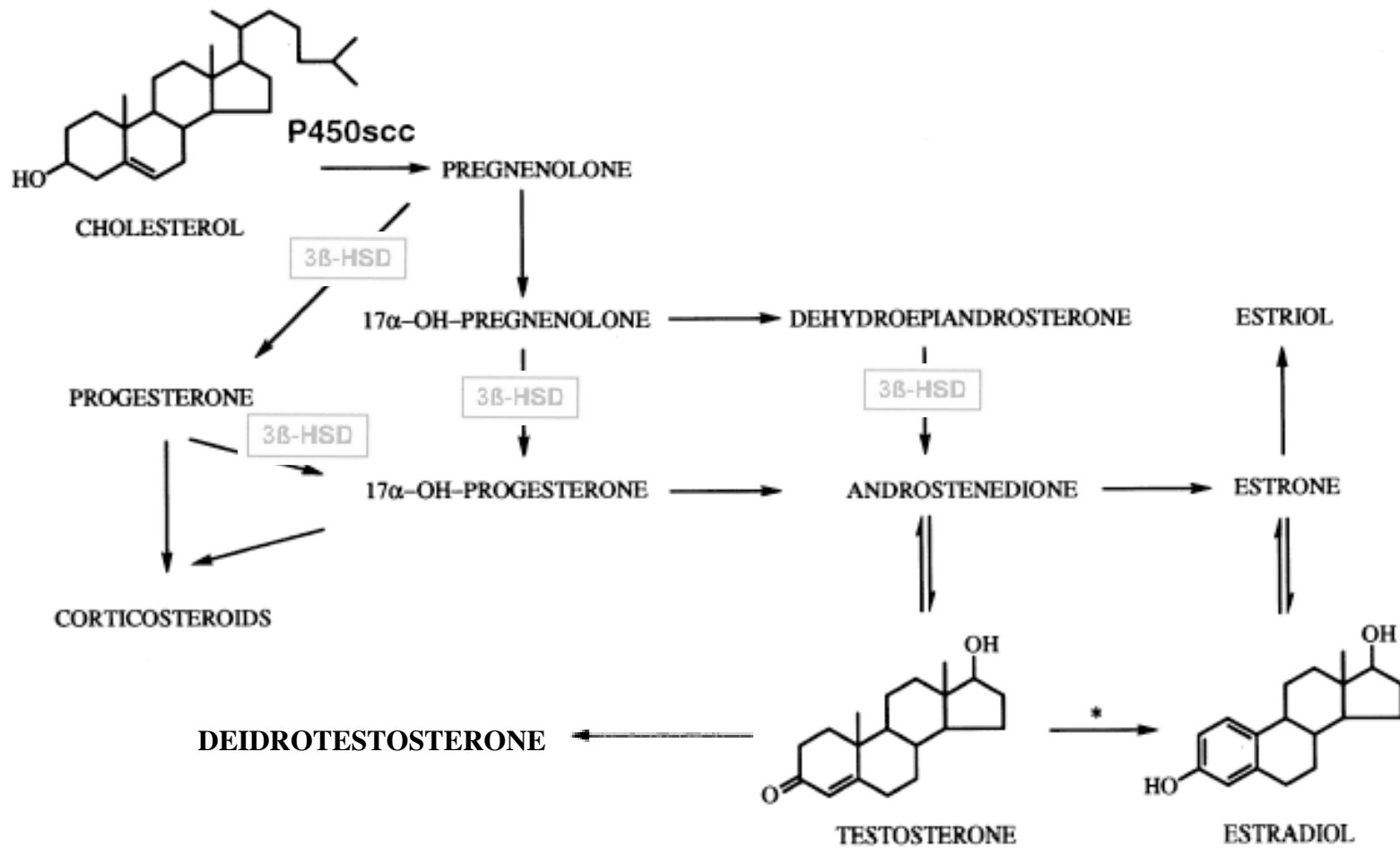


# SINTESI



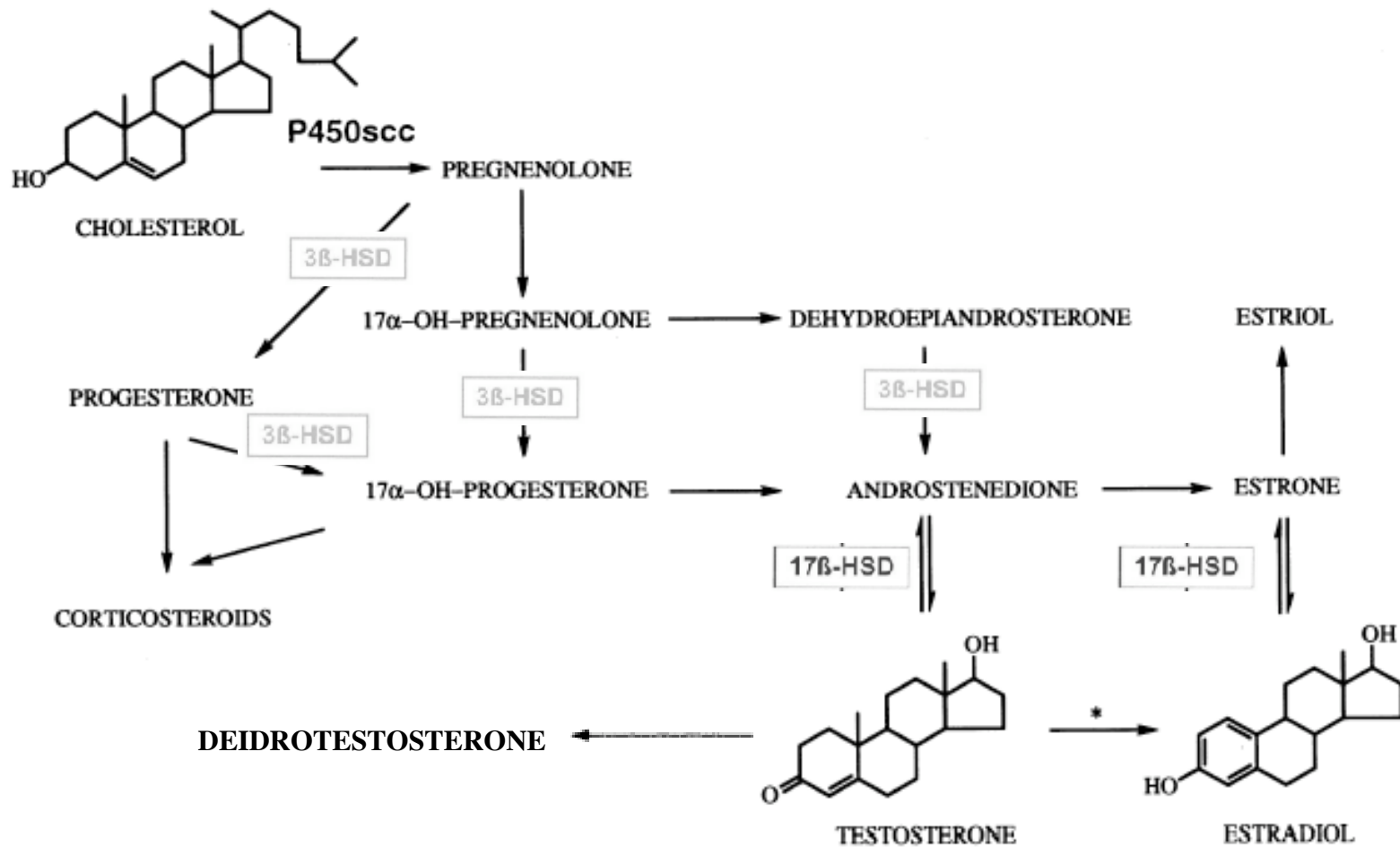
**P450-side chain cleavage enzyme**

# SINTESI



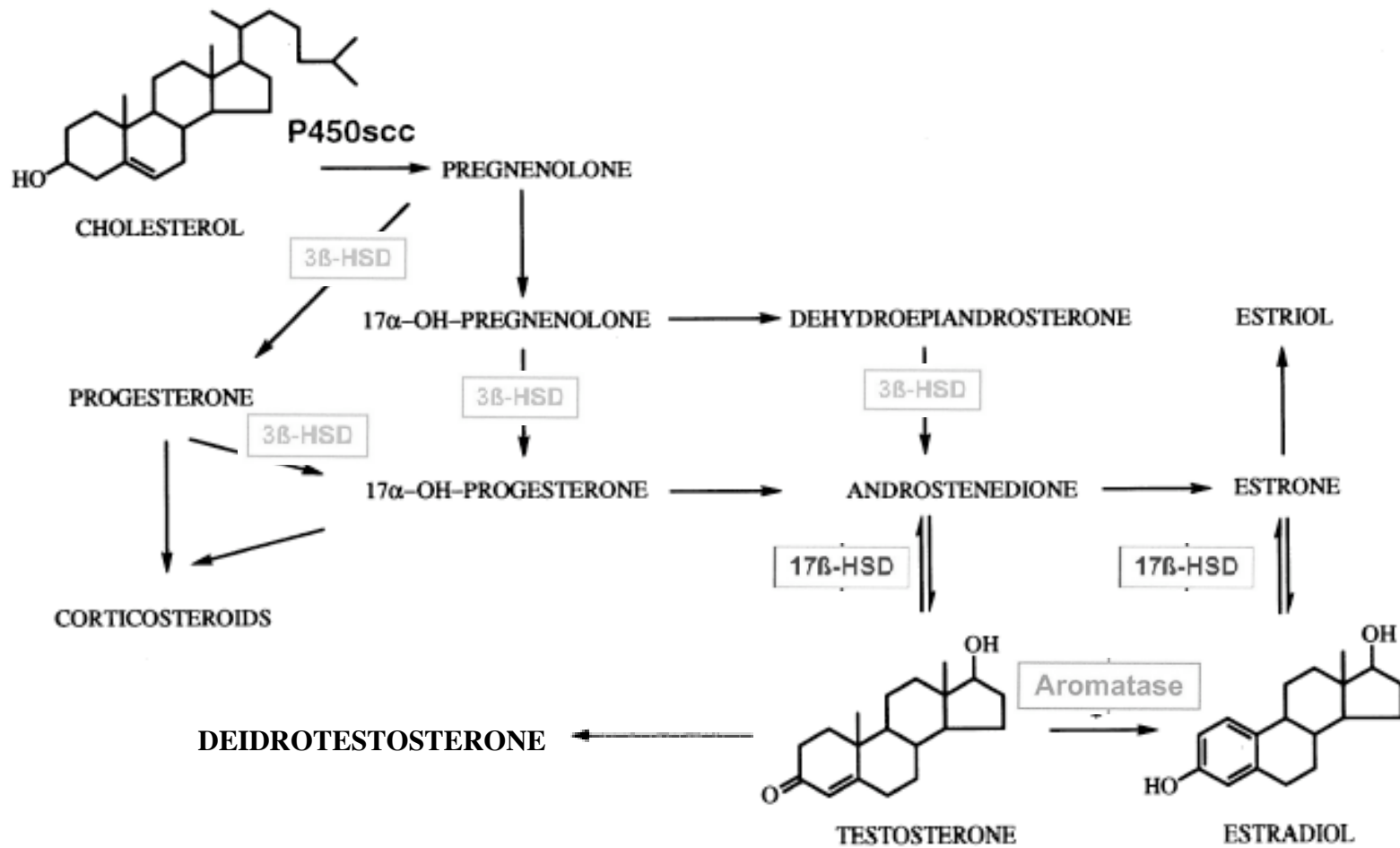
**3-beta idrossisteroide deidrogenasi**

# SINTESI



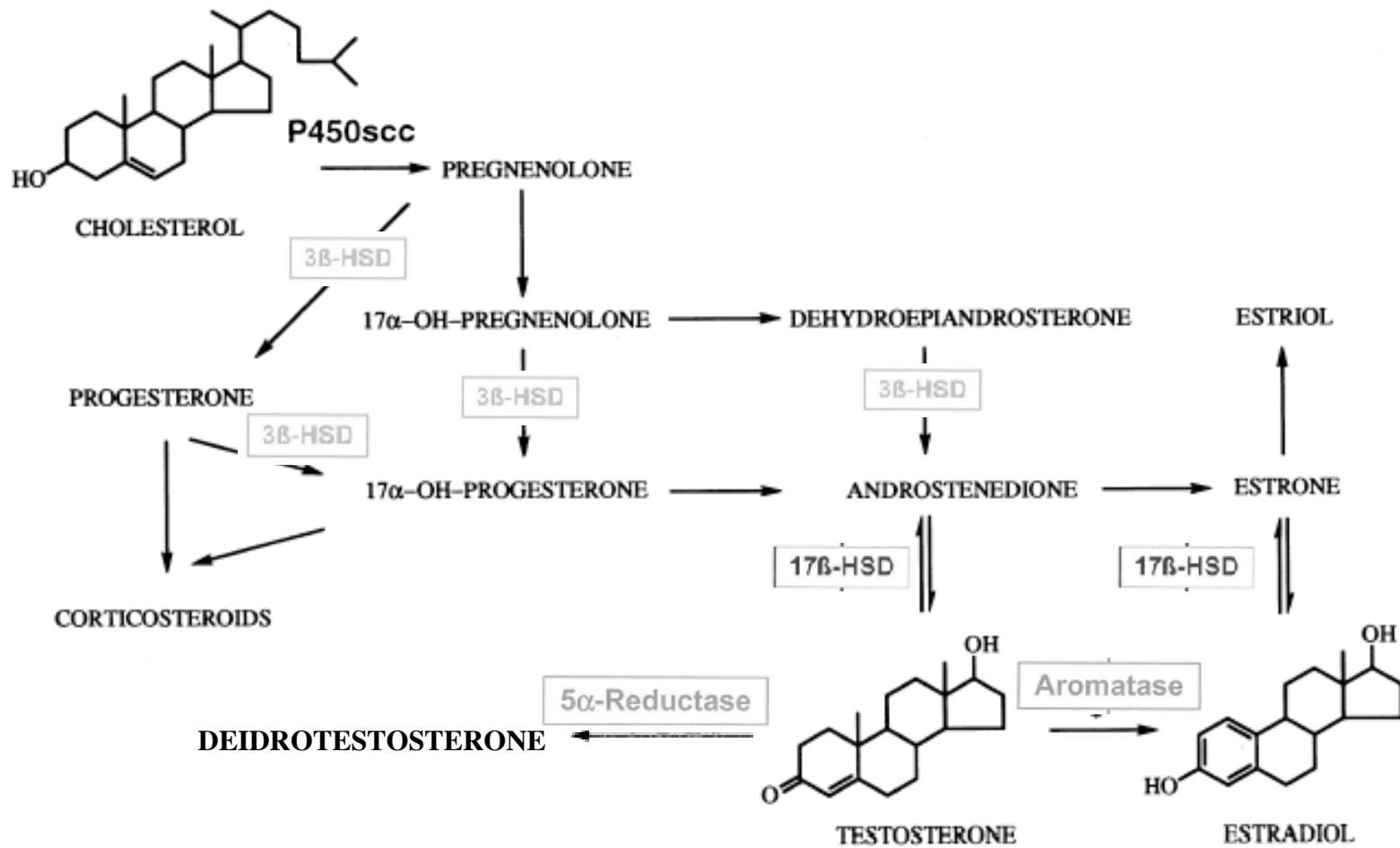
**17-beta idrossisteroide deidrogenasi**

# SINTESI



**aromatasi**

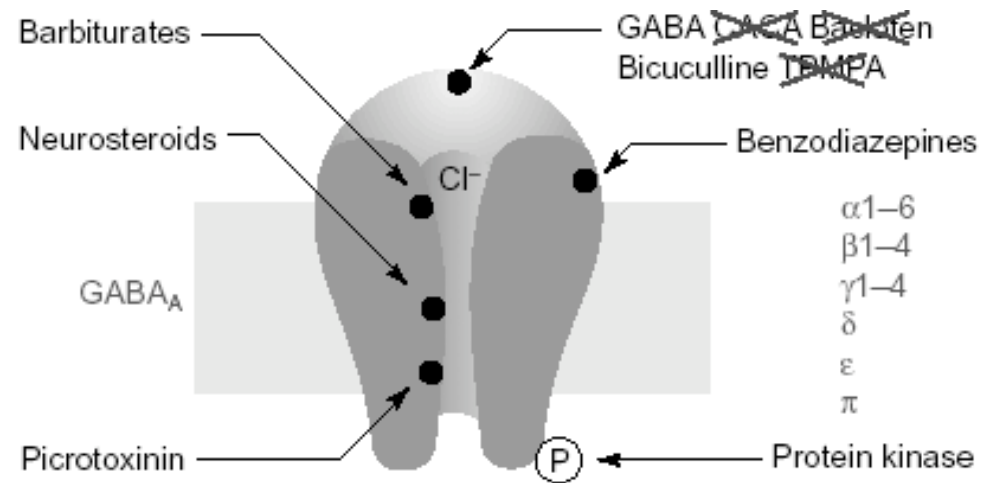
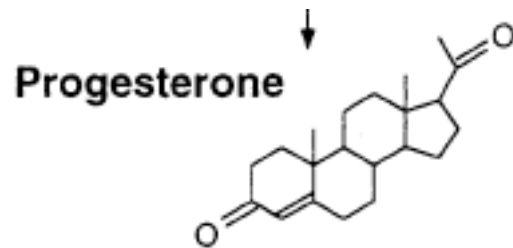
# SINTESI



**5alfa reduttasi**

# PROGESTERONE

- Può legarsi al recettore GABA<sub>A</sub> e modulare la trasmissione GABAergica



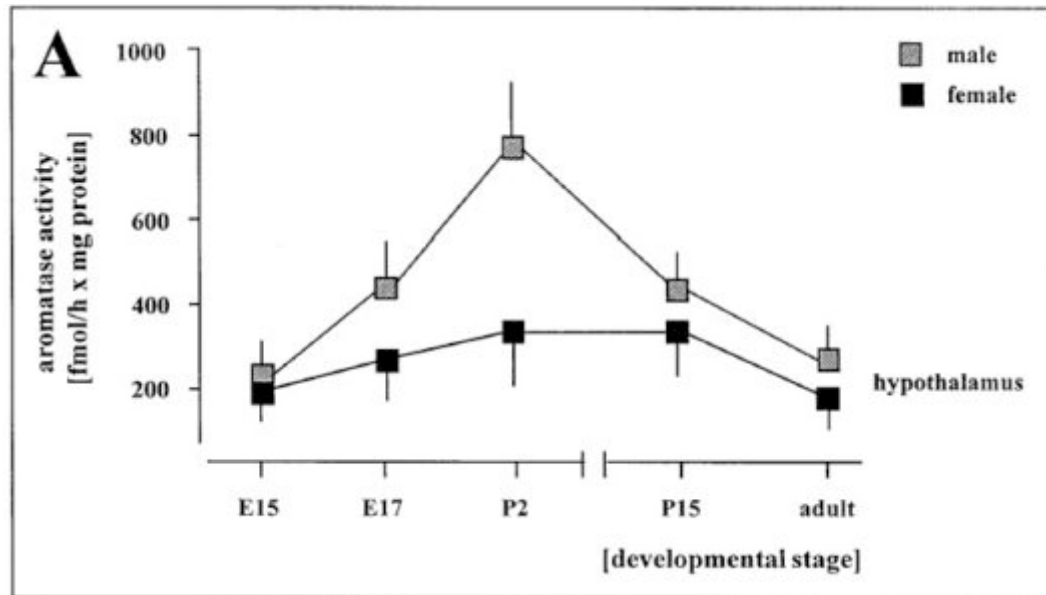
# TESTOSTERONE E DHT

- **Possono legarsi ai recettori per gli androgeni presenti in varie aree encefaliche**

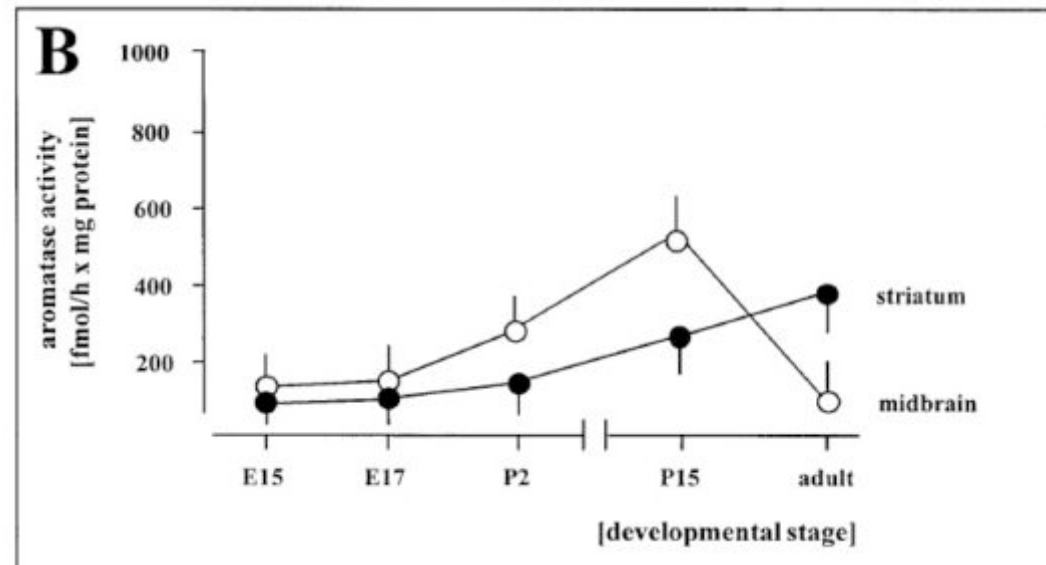
# **ESTRADIOLO**

- **Può legarsi ai recettori per gli estrogeni diffusi in numerosissime regioni cerebrali**
- **Può legarsi a recettori di membrana e dare origine ad effetti a brevissimo o a breve termine**

## VARIAZIONI DELL'ATTIVITA' AROMATASICA NEL CORSO DELLO SVILUPPO

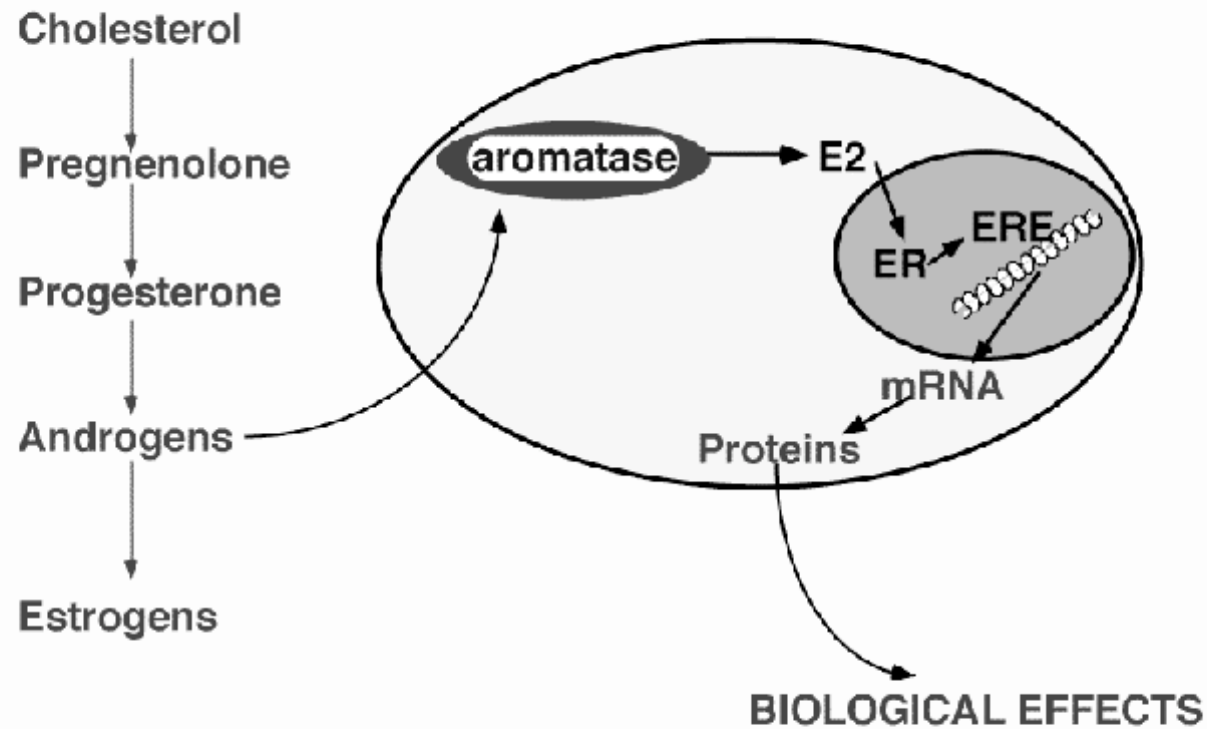


**Gli enzimi che servono alla sintesi dei neurosteroidi possono avere una espressione diversa a seconda della regione e dell'età.**

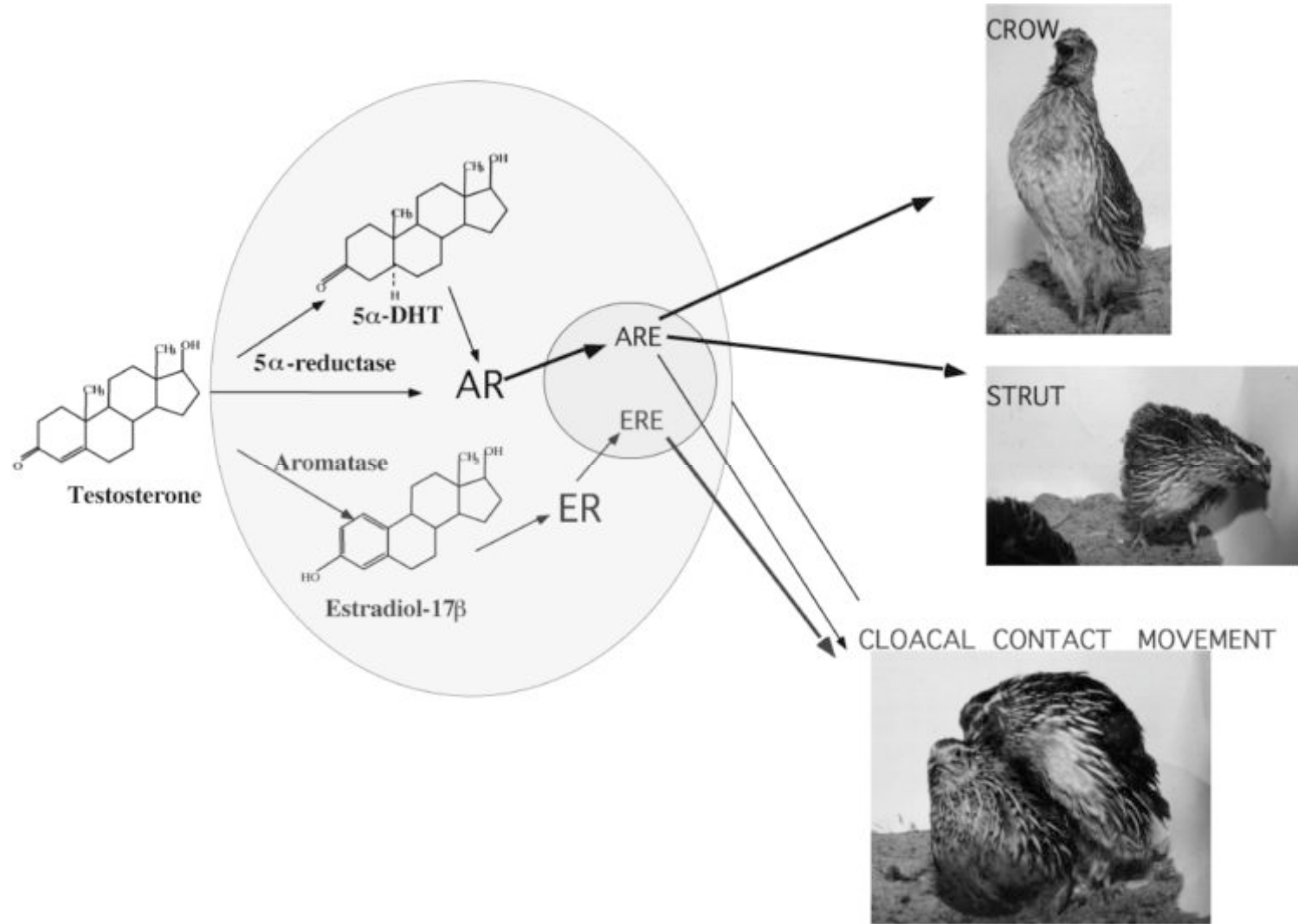


**A. Presenza di dimorfismo nella espressione dell'aromatasi ipotalamica nella prima settimana di vita.**  
**B. Inversione nella quantità di aromatasi tra striato e mesencefalo**

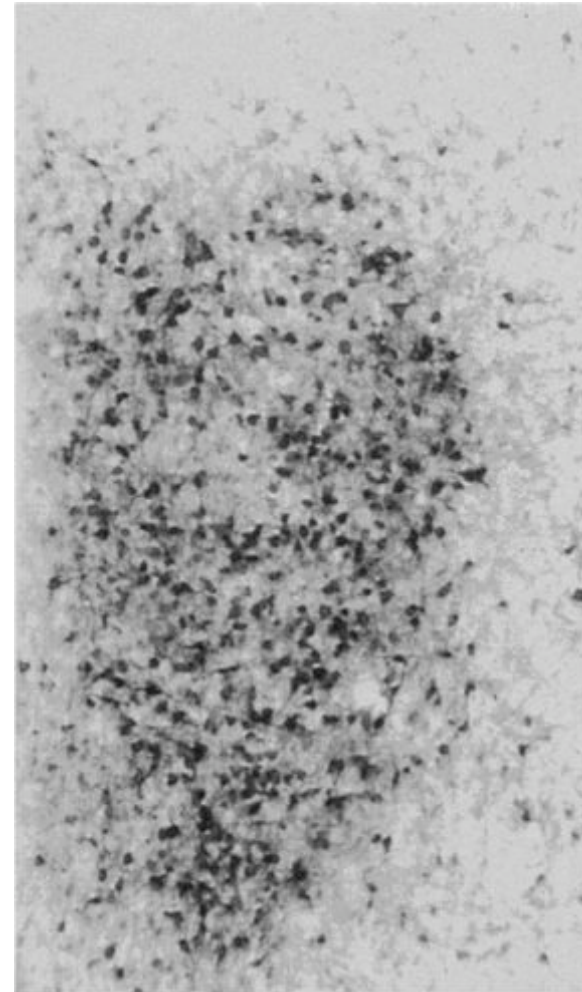
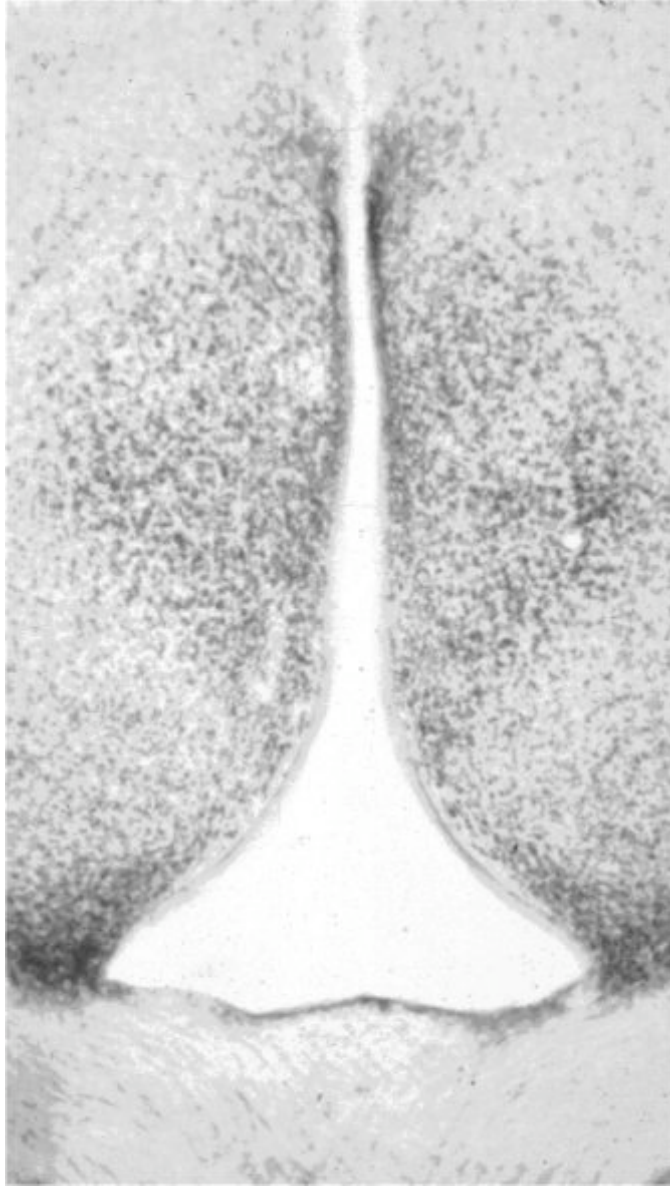
# MOLTI EFFETTI DEL T NEL SNC SONO MEDIATI DA ESTROGENI PRODOTTI LOCALMENTE



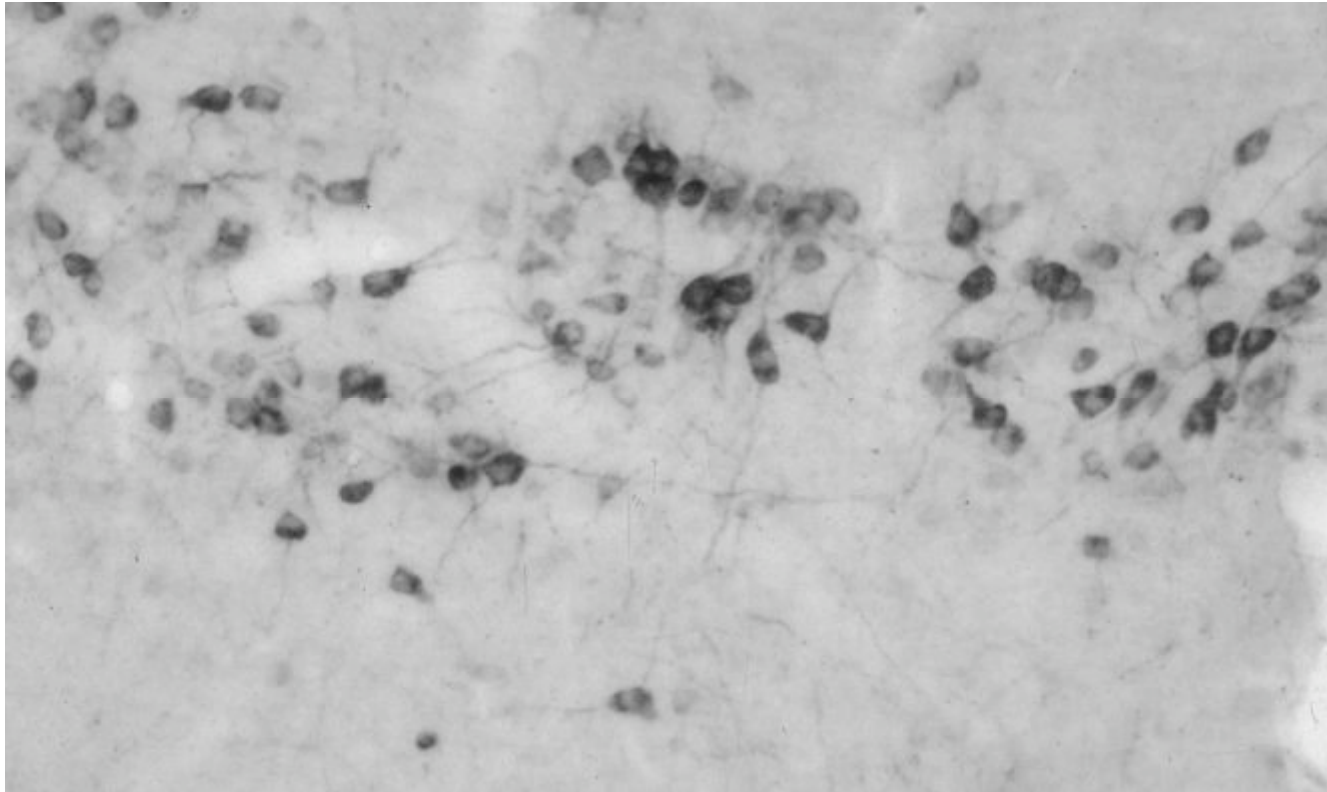
# STEROIDI E COMPORTAMENTO MASCHILE



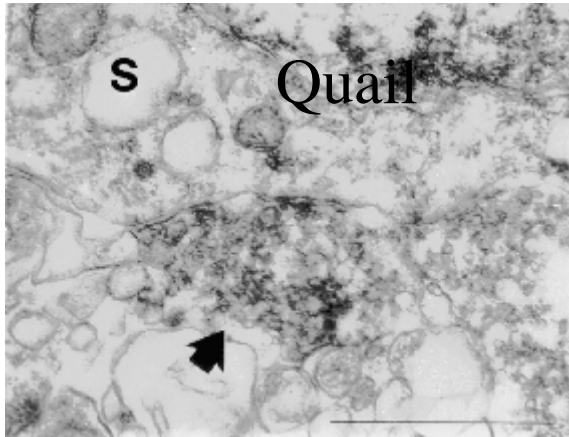
**CELLULE ARO-ir MARCANO  
IN MANIERA SPECIFICA IL  
POM**



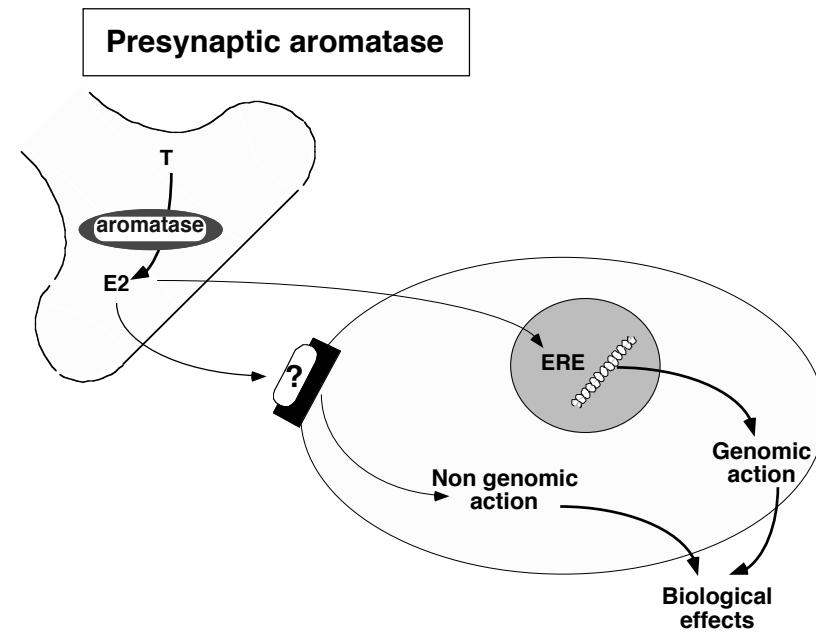
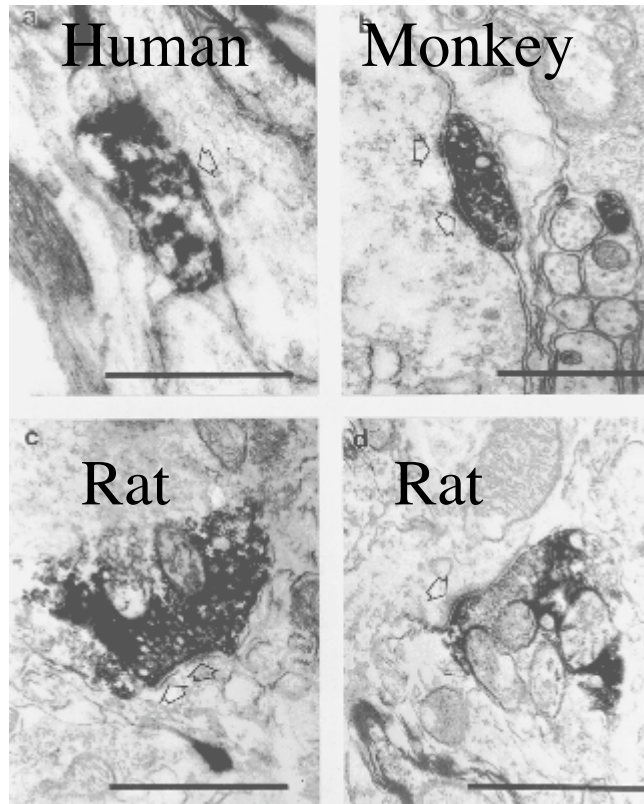
# Organizzazione anatomica: Localizzazione subcellulare



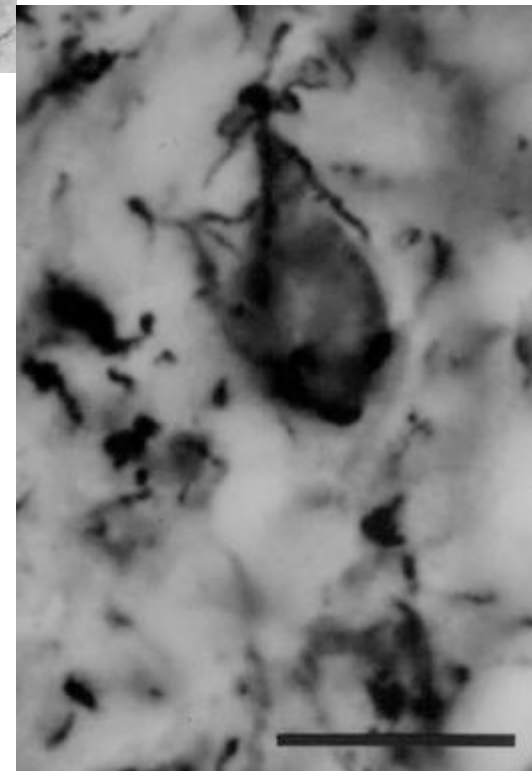
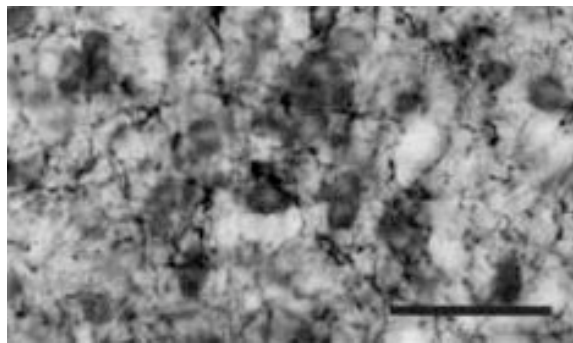
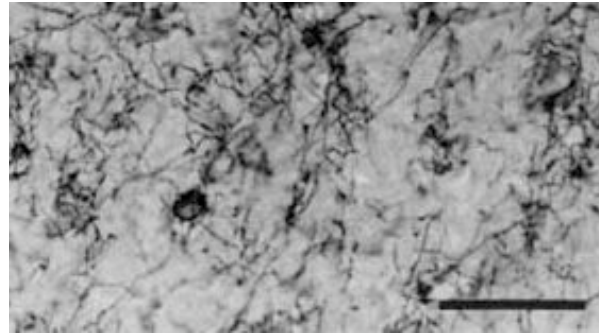
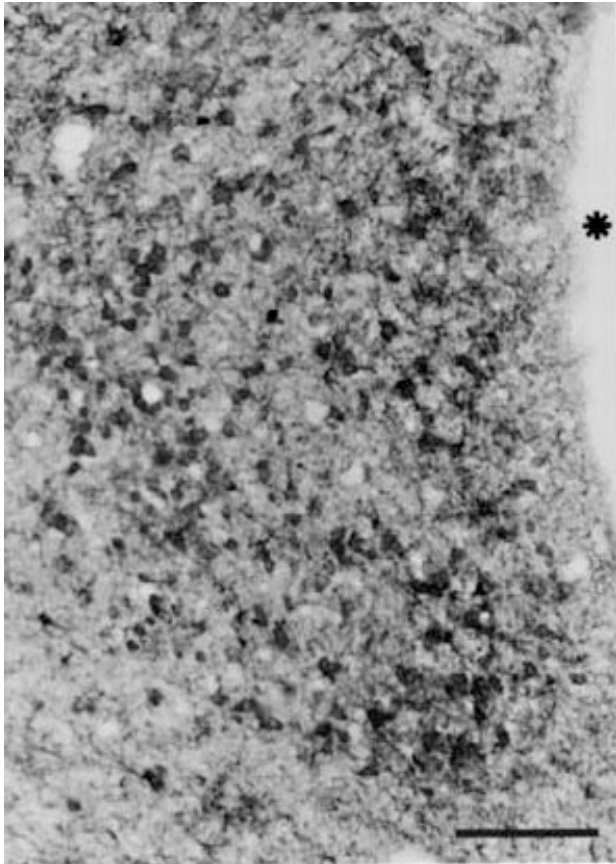
**Corpo cellulare**  
**Processi**



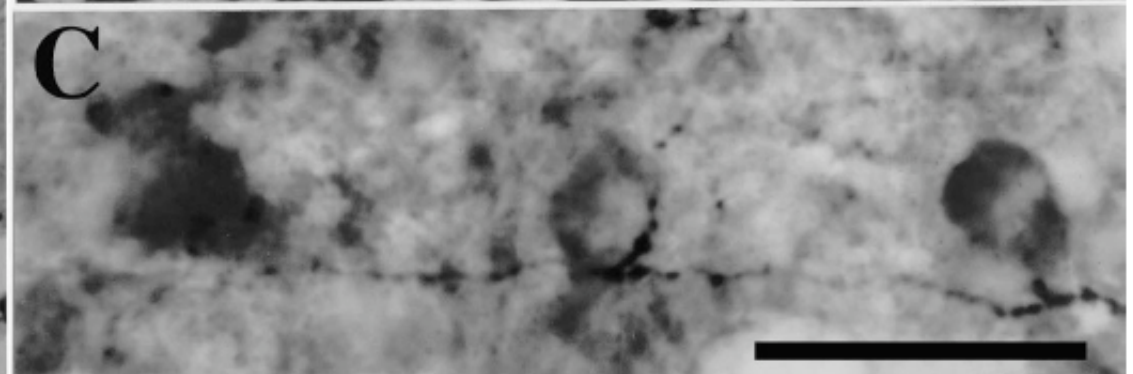
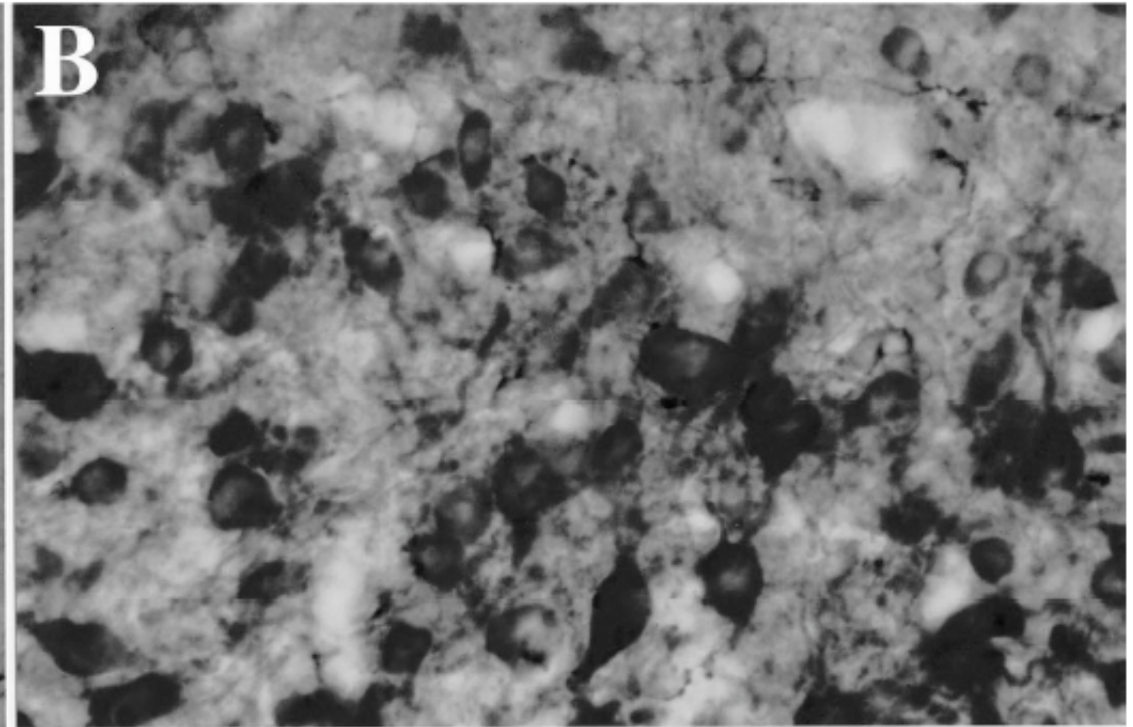
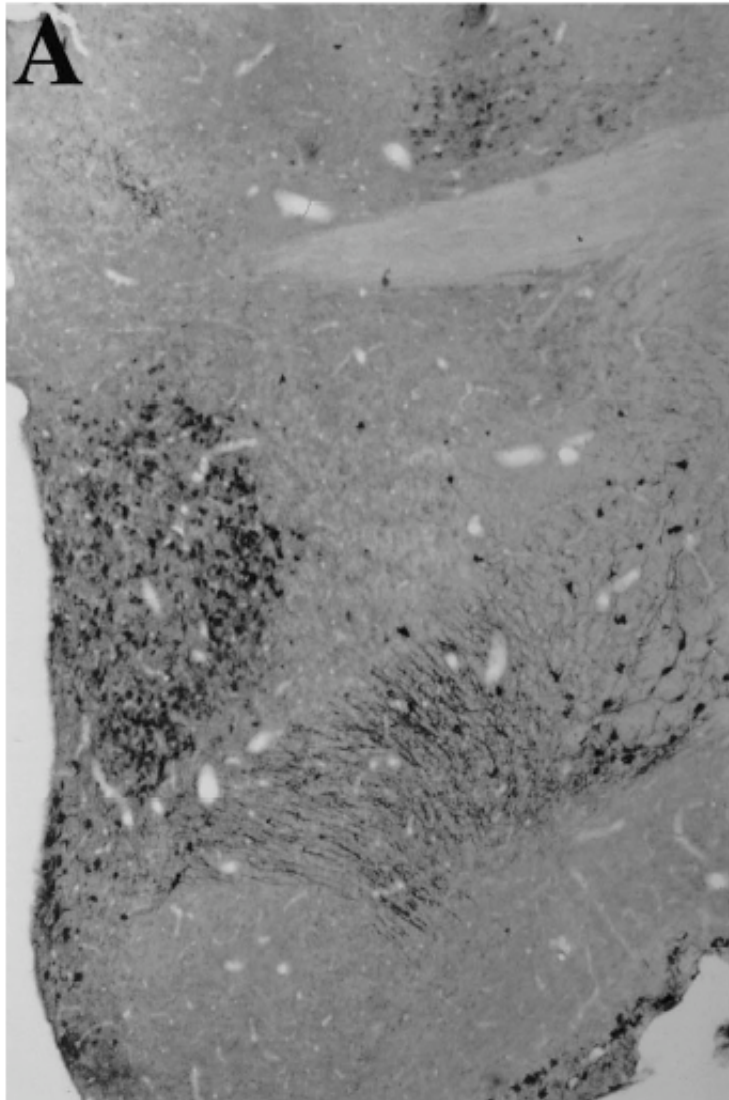
# ARO-ir si trova nei terminali presinaptici



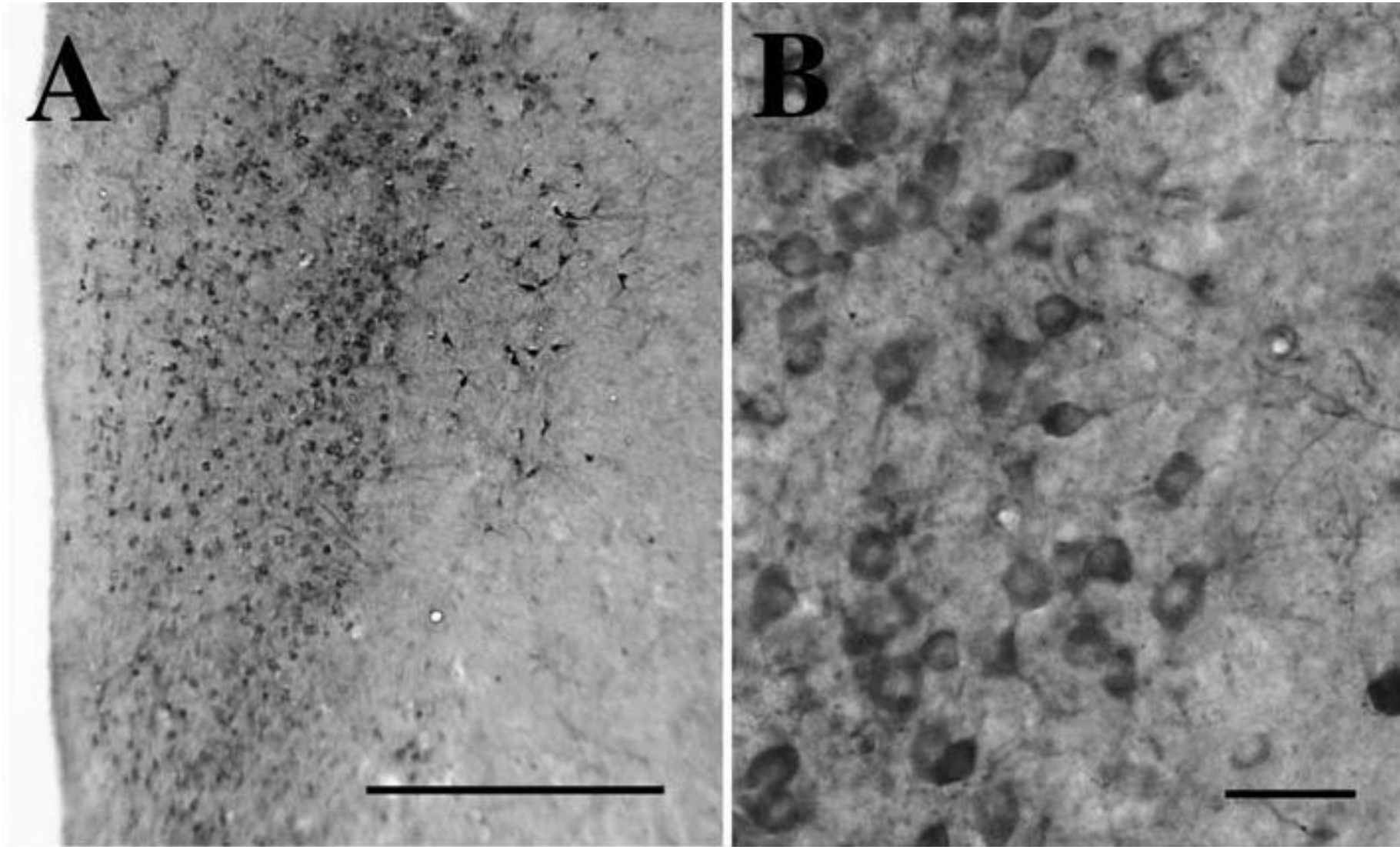
# Innervazione catecolaminergica dei neuroni ARO-ir



# I neuroni ARO-ir sono innervati da fibre a VT



# Innervazione da parte di fibre NOS-ir



# **Afferenze e steroidi sessuali**

- **Le fibre catecolaminergiche provengono dall'Area Ventrale ed in particolare da cellule che presentano recettori per gli estrogeni**
- **Le fibre a VT sono sessualmente dimorfiche e provengono dal BST ove sono molto numerosi i recettori per gli estrogeni e gli androgeni**
- **L'espressione della NOS è a sua volta estrogeno-dipendente.**

